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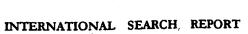
For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR MONITORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY

(57) Abstract: This invention relates to antiviral drug susceptibility and resistance tests to be used in identifying effective drug regimens for the treatment of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), particularly treatment regimes including a protease inhibitor. The invention further relates to the means and methods of monitoring the clinical progression of HIV infection and its response to antiretroviral therapy using phenotypic or genotypic susceptibility assays.





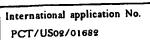




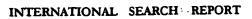
International application No. PCT/US02/01682

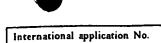
A. CLASSIFICATION OF SUBJECT MATTER 1PC(7) :C12N 9/00, 9/50; C12Q 1/57					
US CL. :435/23, 183, 219					
According to International Patent Classification (IPC) or to both national classification and IPC					
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols)					
U.S.: 485/25, 185, 219					
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched					
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) BIOSIS, MEDLINE, WEST					
C. DOC	UMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where app	propriate, of the relevant passages	Relevant to claim No.		
Y	US 5,837,464 A (CAPON et al) 17 document.	November 1998, see entire	1-6, 10-16 and 20- 23		
Y	YOUNG, B. et al. Resistance Mutation Transcriptase Genes of Human Immu- Isolates from Patients with Combina Failure. Journal of Infectious Diseases. No. 5, pages 1497-1501, see entire doc	nodeficiency Virus Type 1 tion Antiretroviral Therapy November 1998, Vol. 178,	1-6, 10-16 and 20- 23		
X Further documents are listed in the continuation of Box C. See patent family annex.					
Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand to be of particular relevance "X" document of particular relevance; the claimed invention cannot be			plication but caled to understand to invention		
"E" earlier document published on or after the international filling date		"X" document of particular relevance; to considered novel or cannot be considered to the document is taken alone	ered to involve an inventive step		
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Date of the actual completion of the international search Date of mailing of the international search Date of mailing of the international search report 0 9 JUL 2002					
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230 Authorized officer LAURIE SCHEINER Telephone No. (703) 308-0196					





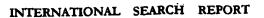
- (ntion). DOCUMENTS CONSIDERED TO BE RELEVANT		Relevant to claim No.	
Category*	Citation of document, with indication, where appropriate, of the relevant p	Relevant to claim 140.		
Y	HERTOGS et al. A Rapid Method for Simultaneous Detection of Phenotypic Resistance to Inhibitors of Protease and Reverse Transcriptase in Recombinant Human Immunodeficiency Virus Type 1 Isolates from Patients Treated with Antiretroviral Drugs. Antimicrobial Agents and Chemotherapy. February 1998, Vol. 42, No. 2, pages 269-276, especially page 270.		1-6, 10-16 and 20-23	
			·. ·	
		4		





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Во	x I O	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)			
Thi	This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:				
1.		Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:			
2.		Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:			
5.		Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).			
Во	× II(Observations where unity of invention is lacking (Continuation of item 2 of first sheet)			
This International Searching Authority found multiple inventions in this international application, as follows:					
	Pl	ease See Extra Sheet.			
		÷			
1.		As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.			
2.		As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.			
3 .		As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:			
4.	X	No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: -6, 10-16 and 20-23 (in-part)			
R	emark	on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.			





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BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 15.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-6, 10-16, 20-23, drawn to a method of ssing the effectiveness of protease antiretroviral therapy by evaluating whether a sample contains a mutation at code 32.

Group II, claim(s) 1-23, drawn to a method of assessing the effectiveness of protease antiretroviral therapy by evaluating whether a sample contains a mutation at codon 90.

Group III, claim(s) 24 and 25, drawn to a resistance test vector encoding a protease with a mutation at codon 82. Group IV, claims 24 and 25, drawn to a resistance test vector encoding a protease with a mutation at codon 90.

The inventions listed as Groups I-IV do not relate to a single inventive concept under PCT Rule 15.1 because, under PCT Rule 15.2, they lack the same or corresponding special technical features for the following reasons: Claim 1 is drawn to a method of assessing the effectiveness of antiretroviral therapy in an HIV-infected patient by evaluating whether a biological sample from the patient has a mutation at codon 82 and a secondary mutation and determining the change in susceptibility to a protease inhibitor. Lorenzi et al. (AIDS. 1997; 11 (12): F95-9, abstract only) teaches collecting samples from HIV-infected patients, sequencing the protease gene after drug therapy, and determining that non-responders developed mutations at codons 82 and 48, which confers resistance to antiviral drugs. Since neither the instant method steps nor the claimed mutations are novel in the art, it is determined that the instant claims lack unity of invention.

Group II is drawn to a second method of evaluating distinct mutations from group I.

Group III is drawn to a first product.

Group IV is drawn to a second product.